SUNESIS.2DV1C1 PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant	:	Wells, et al.	) Group Art Unit Unknown
Appl. No.	:	Unknown (This is a Continuation of copending Application of U.S. Serial No. 09/981,547)	) I hereby certify that this correspondence and all marked attachments are being deposited with the United States Postal Service as first-class mail in an envelope addressed to: Commissioner for Patents, Washington, D.C 20231, on
Filed	:	Herewith	) January 11, 2002 (Date)
For	:	METHODS FOR RAPIDLY IDENTIFYING SMALL ORGANIC MOLECULE LIGANDS FOR BINDING TO BIOLOGICAL TARGET MOLECULES	) Ginger R Dreger, Reg. No. 33,055
Examiner	:	Unknown	

PRELIMINARY AMENDMENT

Commissioner for Patents
Washington, D.C. 20231

Dear Sir:

The present Preliminary Amendment is filed concurrently with the filing of a continuation of copending application Serial No. 09/981,547 filed on October 17, 2001.

Kindly amend this application in the following aspects:

In the Claims:

Please cancel claim 1, without prejudice.

Please add the following new claims:

--40. A process comprising

(a) screening a library of small organic compounds with a target protein-ligand conjugate formed by the covalent bonding of a biological target molecule comprising a first reactive functionality with a compound that comprises (1) a second reactive functionality and (2) a chemically reactive group, wherein the second reactive functionality of the compound reacts

with the first reactive functionality of the biological target molecule to form a first covalent bond such that the protein-ligand conjugate contains a free chemically reactive group, under conditions wherein at least one member of the library forms a second covalent with the target protein-ligand conjugate, and

(b) identifying a small organic compound that binds covalently to the chemically reactive group thereby forming a covalent complex.

41. The process of Claim 40 wherein the second covalent bond is a disulfide bond.

42. The process of Claim 41 wherein the first covalent bond is other than a disulfide bond.

43. The process of Claim 42 wherein the first covalent bond is a thioether.

44. The process of Claim 40 wherein the free chemically reactive group is a thiol.

45. The process of Claim 40 wherein each member of the library of small organic compounds comprises thiols or disulfides.

46. The process of Claim 45 wherein each member of the library further contains a group selected from amides, secondary amines, disulfides and carbamates.

47. The process of Claim 40 wherein the identifying step comprises using mass spectrometry.

48. The process of Claim 47 wherein mass spectrometry is used to measure the mass of complex formed by the small organic compound covalently bound to the target protein-ligand conjugate.

49. The process of Claim 48 wherein the complex is first fragmented prior to subjecting it to mass spectrometry.

50. The process of Claim 49 comprising liberating or releasing the small organic compound for the complex prior to subjecting the small organic molecule to mass spectrometry.

51. The process of Claim 50 wherein the liberating step comprises treating the conjugate with an agent that disrupts the disulfide bond through which the small organic compound forms a complex with the target protein-ligand conjugate.

52. The process of Claim 51 wherein the agent is selected from sodium borohydride or a phosphine such as tris-(2-carboxyethyl)-phosphine (TECP).

53. The process of Claim 51 further comprising coupling the liberated small organic compound to a labeled probe that facilitates identification of the compound by mass spectrometery.

54. The process of Claim 40 wherein the identification step comprises subjecting the complex to NMR.

55. The process of Claim 40 wherein the identification step comprises subjecting the complex to X-ray crystallography.

56. The process of Claim 40 wherein the target protein is selected from enzymes, proteases, kinases, phosphotases (dephosphorylases), cytokine receptors, hormones, interlukins, tyrosine kinase receptors, TNF, mdm2, chemokines and their receptors, signal transduction molecules and transcription factors.

57. A method for identifying a small organic compound that forms a covalent bond with a chemically reactive group on a target biological molecule (TBM) comprising:

(a) obtaining a TBM that comprises or has been modified to comprise a first reactive functionality;

(b) reacting the TBM with a compound that comprises (1) a second reactive functionality and (2) a chemically reactive group, wherein the second reactive functionality reacts with the first reactive functionality of the TBM to form a covalent bond, thereby forming a target molecule comprising the compound linked to the TBM through a covalent bond and providing a free chemically reactive group;

(c) combining the target molecule from (b) with one or more members of a library of organic compounds that are capable of covalently bonding to the chemically reactive group, wherein at least one member of the library forms a covalent bond with the chemically reactive group to from a target molecule/organic compound conjugate; and

(d) identifying the organic compound that forms the covalent bond with the chemically reactive group.

58. The method of Claim 57 wherein the first reactive functionality on the TBM is a cysteine thiol.

59. The method of Claim 58 wherein the covalent bond of step (b) is other than a disulfide bond.

60. The method of Claim 58 wherein the covalent bond of step (b) is a thioether.

Appl. No. :This is a Continuation of copending Application of U.S. Serial No. 09/981,547
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61. The method of Claim 57 wherein the chemically reactive group is a thiol or masked or activated thiol.

62. The method of Claim 57 wherein each member of the library of small organic compounds comprises a thiol or a masked or activated thiol. --

Appl. No. :This is a Continuation of copending Application of U.S. Serial No. 09/981,547
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REMARKS

Prior to entry of the present Preliminary Amendment, claim 1 was pending in this continuing application. Claim 1 has been canceled. New claims 40 through 62 have been added. Support for the new claims is throughout the specification and claims as originally filed, such as, for example, in the paragraph bridging pages 23 and 24; on page 13, line 9 - page 14, line 9; page 18, line 4; page 5, line 18 - page 6, line 9; and page 21, line 1 - page 22, line 9. The new claims do not introduce new matter.

All claims pending in this application are believed to be in *prima facie* condition for allowance, and an early issuance of a Notice of Allowance is respectfully solicited. Should there be any issues outstanding, the Examiner is invited to contact to undersigned attorney at the telephone number indicated below.

Please charge any additional fees, including any fees for additional extension of time, or credit overpayment to Deposit Account No. 11-1410.

Respectfully submitted,

KNOBBE, MARTENS, OLSON & BEAR, LLP

Dated: January 11, 2002

By: _____

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